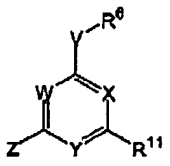
Detailed Description of the Invention

[1] Thus, in a first embodiment, the present invention provides a novel compound of Formula I including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof, comprising:



I

wherein:

V is chosen from $-CHR^5-$, $-NR^5-$, -O-, and –S–;

W, X, and Y are independently chosen from –CH= and –N=;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, $-SR^3$, $-O-R^3$, and $-N(R^1)(R^2)$;

$-N(R^1)(R^2)$ taken together may form a heterocyclyl or substituted heterocyclyl or

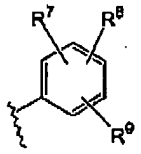
R^1 is chosen from hydrogen, alkyl and subsitituted alkyl; and

R^2 is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^3 is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^5 is chosen from hydrogen and alkyl;

R^6 is



R^7 is chosen from hydrogen, $-N(R^{31})(R^{32})$, halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio;

R^8 is chosen from hydrogen and halogen;

R^9 is chosen from nitro, carboxy, $-C(O)N(R^{31})(R^{32})$, $-SO_2N(R^{31})(R^{32})$,

$-N(R^{33})SO_2R^{34}$, $-C(O)N(R^{33})N(R^{31})(R^{32})$, $-N(R^{33})C(O)R^{34}$, $-CH_2N(R^{33})C(O)R^{34}$, $-N(R^{31})(R^{32})$, $-CH_2OC(O)R^{34}$, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl and $-C(O)R^{10}$;

R^{10} is chosen from heterocyclyl, subsituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, substituted alkyl, and $-N(R^{31})(R^{32})$; or

R^8 and R^9 taken together may form $-C(O)N(R^{33})CH_2-$ or $-C(O)N(R^{33})C(O)-$;

R^{31} and R^{33} are independently chosen from hydrogen,alkyl, and substituted alkyl;

R^{32} is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R^{34} is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

when V is $-NR^5$, $-N(R^5)(R^6)$ taken together may form heterocyclyl or substituted heterocyclyl;

R^{11} is chosen from halogen, OR^{13}, and $-N(R^{12})(R^{13})$;

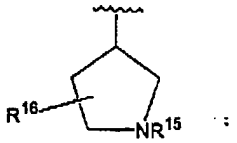
R^{12} is chosen from hydrogen, alkyl, and substituted alkyl;

R^{13} is $-(CH_2)_mR^{14}$;

$-N(R^{12})(R^{13})$ taken together may form a heterocyclyl or substituted heterocyclyl;

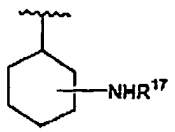
m is 0, 1, 2 or 3;

R^{14} is chosen from hydrogen, alkyl, substituted alkyl, $-C(O)N(R^{31})(R^{32})$, $-N(R^{33})C(O)R^{34}$, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl and



R^{15} is chosen from hydrogen, alkyl, substituted alkyl, alkenyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R^{16} is chosen hydrogen, alkyl, substituted alkyl, and



; or

R^{17} is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and –C(O)-substituted aryl.

[2] In a preferred embodiment, the present invention provides ~~a~~ **the** compound of ~~Claim 1~~ **Formula I** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

two or more of W, Y and X are =N-;

V is $–CHR^5$-, $-NR^5$, or –O-;

Z is $–N(R^1)(R^2)$, -S-aryl, or S-substituted aryl;

R^1 is hydrogen or alkyl;

R^2 is alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl or substituted heterocyclyl;

R^5 is hydrogen;

R^7 is hydrogen, alkyl, substituted alkyl, alkoxy, or halogen;

R^8 is hydrogen;

R^9 is $–C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl or $–N(R^{31})(R^{32})$;

R^{31} is hydrogen, alkyl, or substituted alkyl;

R^{32} is hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl or substituted heterocyclyl;

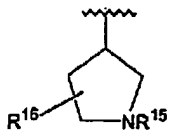
R^{11} is $–N(R^{12})(R^{13})$;

R^{12} is hydrogen, alkyl, or substituted alkyl;

R^{13} is $–(CH_2)_mR^{14}$;

m is 0, 1, 2 or 3;

R^{14} is hydrogen, alkyl substituted alkyl, $-C(O)N(R^{31})(R^{32})$, $-N(R^{33})C(O)R^{34}$, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl or



R^{15} is hydrogen, alkyl or substituted alkyl;

R^{16} is hydrogen or alkyl; or

$-N(R^{12})(R^{13})$ taken together may form a heterocyclyl or substituted heterocyclyl;

R^{33} is hydrogen, alkyl, or substituted alkyl; and

R^{34} is alkyl, substituted alkyl, aryl or substituted aryl.

[3] In a more preferred embodiment, the present invention provides a compound of ~~Claim 2~~ [2] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

two or more of W, Y and X are =N-;

V is –NH-, or –O-;

Z is $-N(R^1)(R^2)$, -S-aryl, or S-substituted aryl;

R^1 is hydrogen or alkyl or 1 to 4 carbons;

R^2 is alkyl or substituted alkyl wherein alkyl is of 1 to 8 carbons;

R^7 is hydrogen, alkyl, of 1 to 4 carbons, alkoxy of 1 to 4 carbons, or halogen;

R^8 is hydrogen;

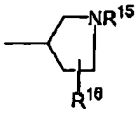
R^9 is $-C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is $-NH_2$, -NH-alkyl, –NH-alkoxy, -NH-phenyl, or $-NH-CH_2$-phenyl wherein alkyl and alkoxy are of 1 to 6 carbons;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2, or 3 additional nitrogen atoms or wherein

R^{12} is hydrogen;

R^{13} is alkyl of 1to 4 carbons or



: and

R^{15} and R^{16} are independently selected from hydrogen and methyl.

[4] In another preferred embodiment, the present invention provides a compound of ~~Claim 3~~ [3] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

W, Y and X are each =N-;

V is –NH-, or –O-;

Z is $-N(R^1)(R^2)$, -S-aryl, or S-substituted aryl;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^7 is hydrogen, methyl, methoxy, Cl, Br, or F;

R^8 is hydrogen;

R^9 is $-C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is $-NH_2$, -NH-alkyl, –NH-alkoxy, -NH-phenyl, or $-NH-CH_2$-phenyl wherein alkyl and alkoxy are of 1 to 6 carbons; and

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2, or 3 additional nitrogen atoms.

[5] In another more preferred embodiment, the present invention provides a compound of ~~Claim 3~~ [3] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

W, Y and X are each =N-;

V is –NH-, or –O-;

Z is $-N(R^1)(R^2)$, -S-aryl, or S-substituted aryl;

R^1 is hydrogen or methyl;

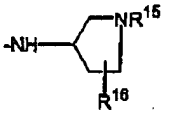
R^2 is alkyl of 1 to 8 carbons;

R^7 is hydrogen, methyl, methoxy, Cl, Br, or F;

R^8 is hydrogen;

R^9 is $-C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is $-NH_2$, -NH-alkyl, –NH-alkoxy, -NH-phenyl, or $-NH-CH_2$-phenyl wherein alkyl and alkoxy are of 1 o 6 carbons;

R^{11} is  ; or –NH-alkyl

wherein alkyl is of 1 to 4 carbons; and

R^{15} and R^{16} are independently selected from hydrogen and methyl.

[6] In another more preferred embodiment, the present invention provides a compound of ~~Claim 4~~ **[4] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof

wherein:

R^{10} is $-NH_2$, $-NH-CH_3$, $-NH-C_2H_5$, $-NH-OCH_3$, or $-NH-OC_2H_5$.

[7] In another more preferred embodiment, the present invention provides a compound of ~~Claim 5~~ **[5] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof

wherein:

R^{10} is $-NH_2$, $-NH-CH_3$, $-NH-C_2H_5$, $-NH-OCH_3$, or $-NH-OC_2H_5$.

[8] In yet another preferred embodiment, the present invention provides a compound of ~~Claim 3~~ **[3] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof

wherein:

two of W, Y and X are each =N- and the other is –CH= ;

V is –NH-, or –O-;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^7 is hydrogen, methyl, methoxy, Cl, Br, or F;

R^8 is hydrogen;

R^9 is $-C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is $-NH_2$, -NH-alkyl, -NH-alkoxy, -NH-phenyl, or $-NH-CH_2$-phenyl wherein alkyl and alkoxy are of 1 to 6 carbons;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2, or 3 additional nitrogen atoms.

[9] In yet another more preferred embodiment, the present invention provides a compound of ~~Claim 8~~ **[8] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^{10} is $-NH_2$, $-NH-CH_3$, $-NH-C_2H_5$, $-NH-OCH_3$, or $-NH-OC_2H_5$.

[10] In yet another preferred embodiment, the present invention provides a compound of ~~Claim 3~~ **[3] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

two of W, Y and X are each =N- and the other is –CH=;

V is –NH-, or –O-;

R^1 is hydrogen or methyl;

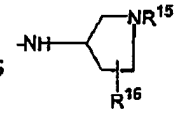
R^2 is alkyl of 1 to 8 carbons;

R^7 is hydrogen, methyl, methoxy, Cl, Br, or F;

R^8 is hydrogen;

R^9 is $-C(O)R^{10}$, heterocyclyl or substituted heterocyclyl;

R^{10} is $-NH_2$, -NH-alkyl, –NH-alkoxy, -NH-phenyl, or $-NH-CH_2$-phenyl wherein alkyl and alkoxy are of 1 to 6 carbons;

R^{11} is  or –NH-alkyl

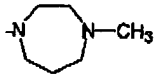
wherein alkyl is of 1 to 4 carbons; and

R^{15} and R^{16} are independently selected from hydrogen and methyl.

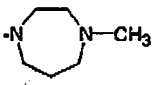
[11] In yet another preferred embodiment, the present invention provides a compound of ~~Claim 10~~ **[10] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^{10} is $–NH_2$, $-NH-CH_3$, $–NH-C_2H_5$, $-NH-OCH_3$, or $–NH-OC_2H_5$.

[12] In yet another preferred embodiment, the present invention provides a compound of ~~Claim 4~~ **[4] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^{11} is 

[13] In yet another preferred embodiment, the present invention provides a compound of ~~Claim 8~~ **[8] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^{11} is 

[14] In a second preferred embodiment, the present invention provides a pharmaceutical composition comprising as an active ingredient, ~~a~~ **the** compound **of Formula I**, or a prodrug or salt thereof and a pharmaceutically acceptable carrier.

[15] In a more preferred embodiment, the present invention provides a pharmaceutical composition according, further comprising one or more additional active ingredients.

[16] In a more preferred embodiment, the present invention provides a pharmaceutical composition wherein said additional active ingredient is an anti-inflammatory compound or an immunosuppressive agent.

[17] In a preferred embodiment, the present invention provides a pharmaceutical composition wherein said additional active ingredient is chosen from a steroid and an NSAID.

[18] In a third preferred embodiment, the present invention provides a method of inhibiting TNF-α expression in a mammal, the method comprising administering to the mammal an effective amount of a composition according to ~~Claim 14~~ **[14] above**.

[19] In a more preferred embodiment, the present invention provides a method of treating TNF-α mediated disorder, the method comprising administering to a mammal in need of such treatment, an effective amount of a composition according to ~~Claim 14~~ **[14] above**.

[20] In a more preferred embodiment, the present invention provides a method of treating TNF-α mediated disorder, wherein the TNF-α mediated disorder is an inflammatory disorder.

[21] In a even more preferred embodiment, the present invention provides a method of treating TNF-α mediated disorder, wherein the TNF-α mediated disorder is chosen from bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease states, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion

injury, renal reperfusion injury, thrombus, glomerulonephritis, Chron's disease, ulcerative colitis, inflammatory bowel disease, multiple sclerosis, endotoxin shock, osteoporosis, Alzheimer's disease, congestive heart failure and cachexia.

[22] In a more preferred embodiment, the present invention provides a method of treating TNF-α mediated disorder wherein the pharmaceutical composition of the invention is administered with one or more additional anti-inflammatory or immunosuppressive agents as a single dose form or as separate dosage forms.

[23] In an even more preferred embodiment, the present invention provides a method of treating a condition associated with TNF-α expression in a mammal, the method comprising administering to a mammal in need of such treatment, an effective amount of a composition according to ~~Claim 14~~ [14] above.

[24] In an even more preferred embodiment, the present invention provides a method of treating a condition associated with TNF-α expression in a mammal wherein the condition associated with TNF-α expression is an inflammatory disorder.

[25] In a even more preferred embodiment, the present invention provides a method of treating a condition associated with TNF-α expression in a mammal wherein the condition associated with TNF-α expression is chosen from bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease states, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Chron's disease, ulcerative colitis, inflammatory bowel disease, multiple sclerosis, endotoxin shock, osteoporosis, Alzheimer's disease, congestive heart failure and cachexia.

[26] In a more preferred embodiment, the present invention provides a method of treating a condition associated with TNF-α expression in a mammal wherein the

pharmaceutical composition of the invention is administered with one or more additional anti-inflammatory or immunosuppressive agents as a single dose form or as separate dosage forms.

[27] In yet another more preferred embodiment, the present invention provides a method of treating a condition associated with p38 kinase activity in a mammal, the method comprising administering to a mammal in need of such treatment, an effective amount of a composition according to ~~claim 14~~ [14] above.

[28] In yet another more preferred embodiment, the present invention provides a method of treating a condition associated with p38 kinase activity in a mammal, wherein the condition associated with p38 kinase activity is an inflammatory disorder.

[29] In yet another more preferred embodiment, the present invention provides a method of treating a condition associated with p38 kinase activity in a mammal, wherein the condition associated with p38 kinase activity is chosen from bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease states, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Chron's disease, ulcerative colitis, inflammatory bowel disease, multiple sclerosis, endotoxin shock, osteoporosis, Alzheimer's disease, congestive heart failure and cachexia

[30] In yet another more preferred embodiment, the present invention provides a method of treating a condition p38 kinase activity in a mammal wherein the pharmaceutical composition of the invention is administered with one or more additional anti-inflammatory or immunosuppressive agents as a single dose form or as separate dosage forms.

[31] In a further preferred embodiment, the present invention provides ~~a~~ the compound of ~~Claim 1~~ Formula I including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

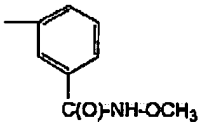
two or more of W, X and Y are –N= .

[32] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

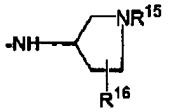
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

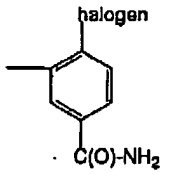
R^{15} and R^{16} are independently hydrogen or methyl.

[33] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

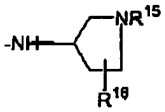
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

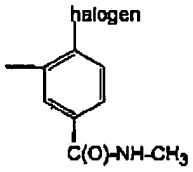
R^{15} and R^{16} are independently hydrogen or methyl.

[34] In a further preferred embodiment, the present invention provides a compound of ~~claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

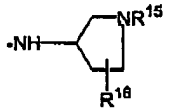
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

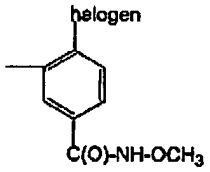
R^{15} and R^{16} are independently hydrogen or methyl.

[35] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

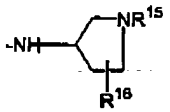
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



: and

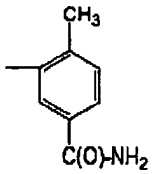
R^{15} and R^{16} are independently hydrogen or methyl.

[36] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

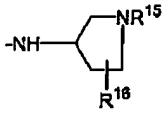
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

:

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

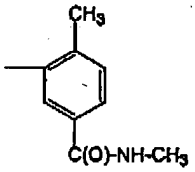
R^{15} and R^{16} are independently hydrogen or methyl.

[37] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

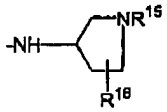
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

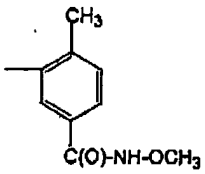
R^{15} and R^{16} are independently hydrogen or methyl.

[38] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

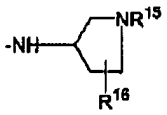
V is –NH- or –O-;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is  :

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or

 : and

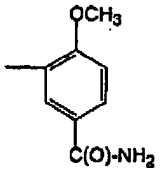
R^{15} and R^{16} are independently hydrogen or methyl.

[39] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

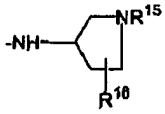
V is –NH- or –O-;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is  :

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or

 : and

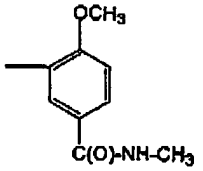
R^{15} and R^{16} are independently hydrogen or methyl.

[40] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

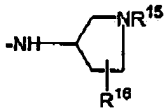
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

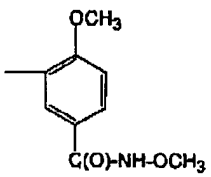
R^{15} and R^{16} are independently hydrogen or methyl.

[41] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ [31] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

V is –NH- or –O-;

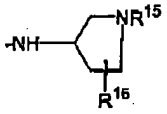
R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is 

;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

R^{15} and R^{16} are independently hydrogen or methyl.

[42] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 31~~ **[31] above** including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

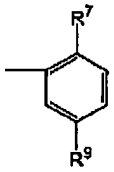
V is –NH- or –O-;

Z is–$N(R^1)(R^2)$;

R^1 is hydrogen or methyl;

R^2 is alkyl of 1 to 8 carbons;

R^6 is

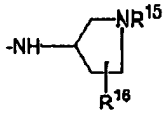


;

R^7 is hydrogen, methyl, methoxy, halogen or cyano;

R^9 is chosen from unsubstituted or substituted triazole, oxadiazole, imidazole, thiazole or benzimidazole;

R^{11} is $-N(R^{12})(R^{13})$ wherein $N(R^{12})(R^{13})$ taken together form a monocyclic heteroocyclyl or substituted heterocyclyl of 5 to 7 atoms containing 1, 2 or 3 additional nitrogen atoms, -NH-alkyl wherein alkyl is of 1 to 4 carbons, or



; and

R^{15} and R^{16} are independently hydrogen or methyl.

[43] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted 1,2,4-triazole.

[44] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted 1,2,4-triazole connected via a C3 or C5 position.

[45] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted 1,2,4-triazole connected via an N4, N1 or N2 position.

[46] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted thiazole connected via a C2 position.

[47] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted thiazole connected via a C4 position.

[48] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted thiazole connected via a C5 position.

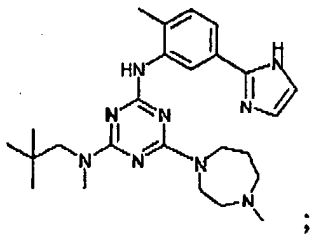
[49] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted 1,3,4-oxdiazole connected via a 2 or 5 position.

[50] In a further more preferred embodiment, the present invention provides a compound of ~~Claim 42~~ [42] above including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates thereof wherein:

R^9 is substituted or unsubstituted imidazole connected via a C2, C5, N1 or N3 position.

[51] In a fourth embodiment, the present invention provides a compound including isomers, enantiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates selected from:



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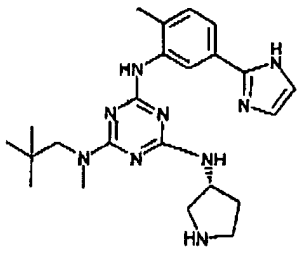
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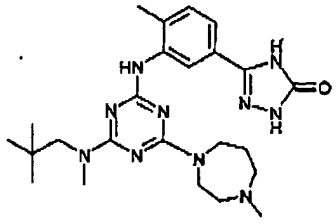
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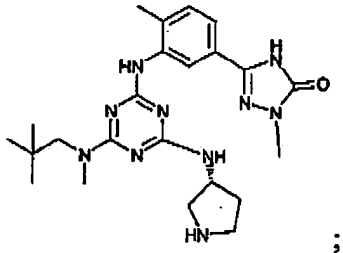
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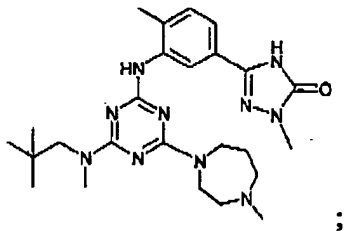
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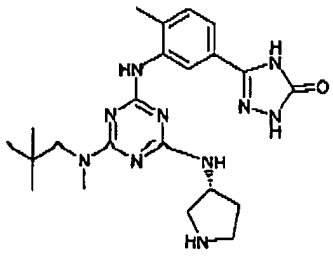
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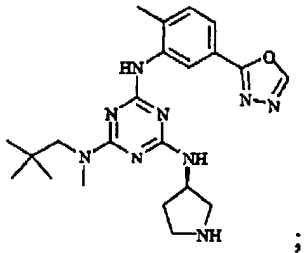

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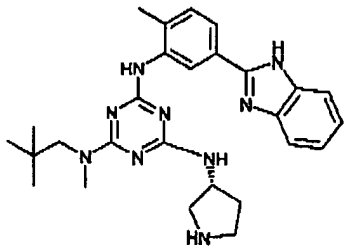

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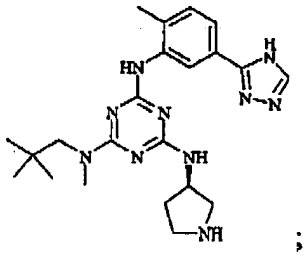

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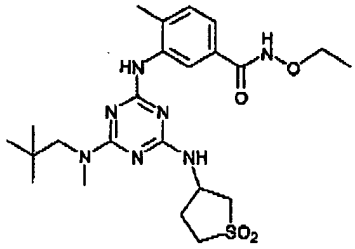

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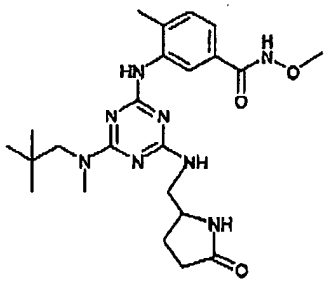

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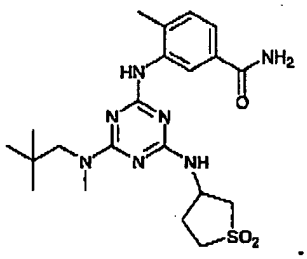

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